

CLAIMS

WHAT IS CLAIMED IS:

1. A human antibody that specifically binds to c-erbB-2, said antibody being a C6 antibody.
- 5 2. The antibody of claim 1, wherein said antibody has the variable heavy (VH) chain of C6.5.
3. The antibody of claim 1, wherein said antibody has the variable light (VH) chain of C6.5.
4. The antibody of claim 1, wherein said antibody is C6.5.
- 10 5. The antibody of claim 1, wherein said antibody has the amino acid sequence of C6.5.
6. The antibody of claim 1, wherein said antibody has the amino acid sequence of C6ML3-14.
7. The antibody of claim 1, wherein said antibody has the amino acid
15 sequence of C6L1.
8. The antibody of claim 1, wherein said antibody has the amino acid sequence of C6MH3-B1.
9. The antibody of claim 1, wherein said antibody has the amino acid sequence of C6ML3-9.

10. The antibody of claim 1, wherein said antibody is selected from the group consisting of an antibody having a V_L domain with one of the amino acid sequences shown in Table 10, an antibody having a V_H domain with one of the amino acid sequences shown in Table 12, an antibody having a V_L CDR3 domain having one of the amino acid sequences shown in Tables 4, 15, and 16, and an antibody having a V_H CDR3 domain having one of the amino acid sequences shown in Tables 13 and 14.
11. The antibody of claim 1, wherein said antibody expressed by any of the clones listed in Table 16.
12. The antibody of claim 1, wherein said antibody is an Fab.
13. The antibody of claim 1, wherein said antibody is an (Fab')₂.
14. The antibody of claim 1, wherein said antibody is (sFv')₂.
15. The antibody of claim 14, wherein said (Sfv')₂ is a fusion protein of two sFv • fragments.
16. The antibody of claim 1, wherein said antibody is C6.5 Fab.
17. The antibody of claim 1, wherein said antibody is C6.5(Fab')₂.
18. The antibody of claim 1, wherein said antibody is C6.5(sFv')₂.
19. The antibody of claim 1, wherein said antibody has a K_d ranging from about 1.6×10^{-8} M to 1.0×10^{-11} M in SK-BR-3 using a Scatchard assay or against purified c-erbB-2 by surface plasmon resonance in a BIAcore.
20. The antibody of claim 1, wherein said K_d is about 1.6×10^{-8} M.
21. A nucleic acid encoding a human C6 antibody that specifically binds to c-erbB-2.
22. The nucleic acid of claim 21, wherein said C6 antibody binds to SK-BR-3 cells with a K_d less than about 1.6×10^{-8} as determined using a scatchard assay.
23. The nucleic acid of claim 21, wherein said nucleic acid encodes an antibody selected from the group consisting of an antibody having a V_L domain containing

one of the amino acid sequences shown in Table 10, an antibody having a V_H domain containing one of the amino acid sequences shown in Table 12, an antibody having a V_L CDR3 domain containing one of the amino acid sequences shown in Tables 4, 15, and 16, and an antibody having a V_H CDR3 domain containing one of the amino acid sequences shown in
5 Tables 13 and 14.

24. The nucleic acid of claim 21, wherein said nucleic acid encodes the variable light (V_L) chain of C6.5.

25. The nucleic acid of claim 21, wherein said nucleic acid encodes the variable heavy (V_H) chain of C6.5.

10 26. The nucleic acid of claim 21, wherein said nucleic acid encodes C6.5.

27. The nucleic acid of claim 21, wherein said nucleic acid encodes the amino acid of a C6.5 antibody and conservative amino acid substitutions of said C6.5 antibody.

15 28. A cell comprising a recombinant nucleic acid that encodes a human antibody that specifically binds c-erbB-2, wherein said antibody is a C6 antibody.

29. A chimeric molecule that specifically binds a tumor cell bearing c-erbB-2, said chimeric molecule comprising an effector molecule attached to a human C6 antibody that specifically binds c-erbB-2.

20 30. The chimeric molecule of claim 29, wherein said C6 antibody is a single chain Fv (sFv).

31. The chimeric molecule of claim 29, wherein said effector molecule is selected from the group consisting of a cytotoxin, a label, a radionuclide, a drug, a liposome, a ligand, and an antibody.

25 32. The chimeric molecule of claim 29, wherein said effector molecule is a *Pseudomonas* exotoxin.

33. The chimeric molecule of claim 29, wherein said chimeric molecule is a fusion protein.

34. A method for making a C6 antibody, said method comprising:
i) providing a phage library presenting a C6.5 variable heavy
(V_H) chain and a multiplicity of human variable light (V_L) chains;

5

ii) panning said phage library on c-erbB-2; and
iii) isolating phage that specifically bind said c-erbB-2.

35. The method of claim 34, further comprising:
iv) providing a phage library presenting a the variable light chain
(V_L) of the phage isolated in step iii and a multiplicity of human variable heavy (V_H) chains;

10

v) panning said phage library on immobilized c-erbB-2; and
vi) isolating phage that specifically bind said c-erbB-2.

36. A method for making a C6 antibody, said method comprising:
i) providing a phage library presenting a C6.5 variable light
(V_L) chain and a multiplicity of human variable heavy (V_H) chains;

15

ii) panning said phage library on immobilized c-erbB-2; and
iii) isolating phage that specifically bind said c-erbB-2.

37. A method for making a C6 antibody, said method comprising:
i) providing a phage library presenting a C6.5 variable light
(V_L) and a C6.5 variable heavy chain encoded by a nucleic acid variable in the sequence
encoding the CDRs such that each phage display a different CDR;

20

ii) panning said phage library on c-erbB-2; and
iii) isolating phage that specifically bind said c-erbB-2.

38. A method for impairing growth of tumor cells bearing c-erbB-2, said
method comprising contacting said tumor with a chimeric molecule comprising a cytotoxin
attached to a human C6 antibody that specifically binds c-erbB-2.

25

39. A method for detecting tumor cells bearing c-erbB-2, said method
comprising contacting said tumor with a chimeric molecule comprising a label attached to a
human C6 antibody that specifically binds c-erbB-2.

40. A polypeptide comprising one or more of the complementarity determining regions (CDRs) whose amino acid sequence contains a CDR sequence selected from the group consisting of the CDRs listed in Tables 4, 10, 12, 13, 14, 15, and 16.

41. A nucleic acid molecule comprising a nucleotide sequence encoding a single chain polypeptide that exhibits the antibody-binding specificity of a human C6 antibody, said polypeptide comprising:

a) a first polypeptide domain, comprising an amino acid sequence that is the binding portion of a variable region of a heavy chain of a human C6 antibody;

b) a second polypeptide domain, comprising an amino acid sequence that is the binding portion of a variable region of a light chain of a human C6 antibody; and

c) at least one polypeptide linkers comprising an amino acid sequence spanning the distance between the C-terminus of one of the first or second domains and the N-terminus of the other, whereby said linker joins the first and second polypeptide domains into a single chain polypeptide.

42. A polypeptide that exhibits immunological binding properties of a human C6 antibody, said polypeptide comprising first and second domains connected by a linker moiety, wherein:

a) the first domain comprises at least one amino acid sequence that is a CDR derived from a heavy chain of a human C6 antibody; and

b) the second domain comprises at least one amino acid sequence that is a CDR derived from a light chain of a human C6 antibody.

43. The polypeptide of claim 42, wherein the first domain comprises a heavy chain of a human C6 antibody.

44. The polypeptide of claim 42, wherein the second domain comprises a light chain of a human C6 antibody.

45. An expression cassette, comprising:

a) the nucleic acid molecule of claim 41; and

95-276-3

b) a control sequence operably linked to the nucleic molecule and capable of directing the expression thereof.

46. An expression cassette, comprising:

- a) the nucleic acid molecule of claim 41; and
- b) a control sequence operably linked to the nucleic molecule and capable of directing the expression thereof.

47. An expression cassette, comprising:

- a) the nucleic acid molecule of claim 41; and
- b) a control sequence operably linked to the nucleic molecule and capable of directing the expression thereof.

48. A method of inducing the production of a polypeptide, comprising:

a) introducing the expression cassette of claim 47 into a host cell whereby the cassette is compatible with the host cell and replicates in the host cell;

b) growing the host cell whereby the polypeptide is expressed;

c) isolating the polypeptide.

49. A method of inducing the production of a polypeptide, comprising:

a) introducing the expression cassette of claim 47 into a host cell whereby the cassette is compatible with the host cell and replicates in the host cell;

b) growing the host cell whereby the polypeptide is expressed;

c) isolating the polypeptide.

50. A method of inducing the production of a polypeptide, comprising:

a) introducing the expression cassette of claim 47 into a host cell whereby the cassette is compatible with the host cell and replicates in the host cell;

b) growing the host cell whereby the polypeptide is expressed; and

c) isolating the polypeptide.